IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al. Application No.: 10/646,391 Filed: 8/21/2003 Title: Treatment of Melanoma by Reduction in Clusterin Levels Attorney Docket No.: UBC.P-035 Customer No.: 057381	Group Art Unit: 1635 Examiner: Amy Hudson Bowman Confirmation No: 9734

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 CFR 1.144 FOR REVIEW OF RESTRICTION REQUIREMENT

Dear Sir:

Applicants hereby petition pursuant to 37 CFR 1.144 for review of the restriction requirement in the above-referenced application and request a direction to the Examiner to modify the restriction such that election of ten sequences, as opposed to only 1 is permitted, consistent with the provisions in the MPEP.

MPEP § 803.04 (August 2006) indicates that election of ten species of oligonucleotide per application is reasonable even in the context of a composition claim, in accordance with the partial waiver of the single invention provisions of 37 CFR 1.141. Applicants have been required to elect a single oligonucleotide, and the Examiner has provided no reasoning as to why election of ten sequences was not originally allowed. Specifically, the Examiner has not shown that this is an "exceptional case" in which "the complex nature of the claimed material, for example a protein amino acid sequence reciting three dimensional folds, may necessitate that the reasonable number of sequences to be selected be less than ten." MPEP § 803.04.

The claims of the present application are method claims, and independent claim 1 and dependent claims 6 and 12 are representative of the issue presented here. These claims are reproduced here for convenient reference.

> 1. A method for treatment of melanoma in a mammalian subject, comprising the step of administering to the subject a therapeutic agent effective to reduce the amount of clusterin in the melanoma cells.
>
> 6. The method of claim 5, wherein the antisense oligodeoxynucleotide consists essentially of an oligodeoxynucleotide selected from the group consisting of Seq. ID. Nos. 2 to 19.
>
> 12. The method of claim 11, wherein the RNA molecule consists essentially of an oligodeoxynucleotide selected from the group consisting of Seq. ID. Nos.20 to 25.

The antisense oligonucleotide sequences recited in claim 6 are not new, and are disclosed in PCT Publication No. WO 00/049937, US-2002-0128229-A1 and US patent 6, 383,808 (all of which are cited in the application on Page 4 and of record in the prosecution) for the purpose of inhibiting clusterin.

In the restriction requirement mailed February 1, 2005, the Examiner required election of a single nucleotide species, asserting that the lists of sequences in claims 6, 7, 9, 10 and 12 did not constitute a proper genus which could be set forth in a Markush group. Applicants argued against this restriction to the extent that it was other than an election of species in the response filed February 24, 2005. The restriction on the basis of an imprper Markush group was made final in Office Action mailed April 8, 2005.

The Examiner cited MPEP § 803.02 as support for the assertion that the listing of individual sequences was an improper Markush Group. It is noted that MPEP § 803.02 only requires that the different members of Markush group share some **property**, and does not require that this property be structural in nature. Thus, the Examiner has not stated how the Markush groups of the claims that lists multiple sequences does not meet the language that is said to be proper in the MPEP. Furthermore, the Examiner's statement of burden appears to suggest that the claim can only be searched by inserting into the search system each and every one of the recited sequences. Whether of not this is true in the context of a composition claim, Applicants note that the MPEP distinguishes between method claims and composition claims and submits both that this distinction is valid and that it has been ignored by the Examiner.

When discussing method claims, MPEP § 803.02 states that:

> when the Markush group occurs in a claim reciting a process or a combination (not a single compound), it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is mainly responsible for their function in the claimed relationship, and it is clear from their very nature or from the prior art that all of them possess this property.

In this case, all of the oligonucleotides (whether antisense or siRNA) possess the common property of reducing the amount of clusterin in melanoma cells. This property is "mainly responsible" for their usefulness in the claimed method. Accordingly, restriction based on a allegedly improper Markush group is in error.

It is further noted that the MPEP § 808.02 states that

> Where the related inventions as claimed are shown to be independent or distinct under the criteria of MPEP § 806.05(c) - § 806.06, the examiner, in order to establish reasons for insisting upon restriction, **must** explain why there would be a serious burden on the examiner if restriction is not required.

In the present case, it is clearly of record that each of the antisense sequences disclosed in the application is part of the prior art. Thus, **no** searching is required to find these sequences as

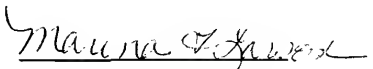
effective in the inhibition of clusterin. The element that needs to be searched is therefore not the sequences, so much as a connection between the inhibition of clusterin and the treatment of melanoma. The Examiner has offered no reasons why such a search poses a burden that is less because of the election of one sequence, as opposed to consideration of all of the sequences. Thus, the assertion of burden is not apparent in this case, where a method claim is presented, and therefore the rejection should be withdrawn.

The final issue to be addressed in this petition is why does the restriction requirement matter, given the presence of linking claims. The answer to this can be found in the Office Action. While the merits of this action will be addressed in the appropriate separate paper, it can be seen that the generic (linking) claim 1 is rejected under 35 USC § 112, first paragraph, as lacking written description support. To the extent that the sequences were treated as species, as opposed to distinct inventions, the Examiner would have had to search the additional sequences, and indicate that they are allowable since they are not subject to the only rejection, or perhaps to posit an additional rejection. The same would be true, albeit to a lesser extent if the examiner at least considered the 10 sequences said to be reasonable by the MPEP. As matters stand, however, the issue of the § 112, first paragraph rejection could proceed to the Board of Appeals and be decided in Applicants favor, at which point in time the Examiner would need to reopen prosecution to consider the other sequences within the scope of the linking claim which could lead to a new rejection and a new appeal. This is not good use of either patent office or applicant resources.

For these reasons, Applicants submit that the restriction requirement in this case is inconsistent with correct practice as defined in the MPEP, and that the Examiner has not established why there is a search burden in this case. Accordingly, an appropriate direction to the

Examiner to modify the restriction requirement and to reopen prosecution accordingly is requested.

Respectfully submitted,



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